SEY 26 1006 SEQUENCE LISTING Kadler, Karl

Kadler, Karl Bulleid, Neil Ashcroft, Gillian

<120> Modified Peptides and Their Uses

<130> 17695-0002

<140> US 10/554,068

<141> 2005-10-21

<150> PCT/GB2004/00171

<151> 2004-04-21

<150> GB 0309064.4

<151> 2003-04-22

<160> 28

<170> PatentIn version 3.3

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His Pro Thr Ile Ile Leu Ala Thr Ser Leu Ser Leu Phe Leu Gln Arg

245 250 255

Leu Asn Ile Glu Asp Gly Lys Leu Met Val Arg Tyr Lys Leu Asn Ser 260 265 270

- Glu Leu Pro Lys Glu Arg Gly Val Gly Asp Ala Ile Asn Asn Gly Arg
 275 280 285
- Asp His Ser Ile Gln Ile Lys Ile Gly Lys Leu Gln Lys Arg Met Trp 290 295 300
- Ile Asn Val Asp Val Gln Asn Thr Ile Ile Asp Gly Glu Val Phe Asp 305 310 315 320
- Phe Ser Thr Tyr Tyr Leu Gly Gly Ile Pro Ile Ala Ile Arg Glu Arg 325 330 335
- Phe Asn Ile Ser Thr Pro Ala Phe Arg Gly Cys Met Lys Asn Leu Lys 340 345 350
- Lys Thr Ser Gly Val Val Arg Leu Asn Asp Thr Val Gly Val Thr Lys 355 360 365
- Lys Cys Ser Glu Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg 370 380
- Gly Gly Gln Leu Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His 385 390 395 400
- Leu Gln Ala Ser Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu 405 410 415
- Leu Asp His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp 420 425 430
- Gly Tyr Ile Glu Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys 435 440 445
- Ser Pro Gln Thr Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile 450 460
- Ser Asp Asn Ser Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg 465 470 475 480

									•						
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Arg	, Lei	1 Sei 515		ı Ser	Pro	Glu	val 520		ı Asp	Leu	ı Thr	Ser 525		ı Sei	c Leu
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Pro	o Ala	a Gl	y Ile 74	e Pro	Gl ₃	y Ph∈	e Pro	Gl _y 745		. Lys	Gly	/ His	750		/ Phe
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Pro	Gly 850	Gln	Arg	Gly	Glu	Pro 855	Gly	Pro	Gln	Gly	His 860	Ala	Gly	Ala	Gln
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- Lys Gly Glu Asp Gly Lys Asp Gly Ser Pro Gly Glu Pro Gly Ala Asn 945 950 955 960
- Gly Leu Pro Gly Ala Ala Gly Glu Arg Gly Ala Pro Gly Phe Arg Gly 965 970 975
- Pro Ala Gly Pro Asn Gly Ile Pro Gly Glu Lys Gly Pro Ala Gly Glu 980 985 990
- Arg Gly Ala Pro Gly Pro Ala Gly Pro Arg Gly Ala Ala Gly Glu Pro 995 1000 1005
- Gly Arg Asp Gly Val Pro Gly Gly Pro Gly Met Arg Gly Met Pro 1010 1015 1020
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- Gly Asn Asp Gly Ala Pro Gly Lys Asn Gly Glu Arg Gly Gly Pro 1070 1075 1080
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- Gly Pro Gln Gly Pro Pro Gly Pro Thr Gly Pro Gly Gly Asp Lys 1100 1105 1110
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1145	1150	1155

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<211> 1604

<212> PRT

<213> Artificial Sequence

<220>

<223> Sequence of modified pro-alpha chain.

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His Pro Thr Ile Ile Leu Ala Cys Ser Glu Asp Trp Lys Leu Val Arg
20 25 30

Ser Ala Ser Phe Ser Arg Gly Gly Gln Leu Ser Phe Thr Asp Leu Gly 35 40 45

Leu Pro Pro Thr Asp His Leu Gln Ala Ser Phe Gly Phe Gln Thr Phe 50 55 60

Gln Pro Ser Gly Ile Leu Leu Asp His Gln Thr Trp Thr Arg Asn Leu 65 70 75 80

Gln Val Thr Leu Glu Asp Gly Tyr Ile Glu Leu Ser Thr Ser Asp Ser 85 90 95

Gly Gly Pro Ile Phe Lys Ser Pro Gln Thr Tyr Met Asp Gly Leu Leu 100 105 110

His Tyr Val Ser Val Ile Ser Asp Asn Ser Gly Leu Arg Leu Leu Ile 115 120 125

Asp	Asp 130		. Leu	Leu	Arg	Asn 135		Lys	Arg	, Leu	Lys 140		Ile	e Ser	Ser
Ser 145	Arg	Gln	Ser	Leu	Arg 150	Leu	Gly	Gly	Ser	Asn 155		Glu	Gly	· Cys	Ile 160
Ser	Asn	Val	Phe	Val 165		Arg	Leu	Ser	Leu 170		Pro	Glu	Val	Leu 175	Asp
Leu	Thr	Ser	Asn 180	Ser	Leu	Lys	Arg	Asp 185	Val	Ser	Leu	Gly	Gly 190	_	Ser
Leu	Asn	Lys 195	Pro	Pro	Phe	Leu	Met 200		Leu	Lys	Gly	Ser 205		Arg	Phe
Asn	Lys 210	Thr	Lys	Thr	Phe	Arg 215	Ile	Asn	Gln	Leu	Leu 220	Gln	Asp	Thr	Pro
Val 225	Ala	Ser	Pro	Arg	Ser 230	Val	Lys	Val	Trp	Gln 235	Asp	Ala	Asn	Gly	Gln 240
Gly	Pro	Gln	Gly	Pro 245	Lys	Gly	Asp	Pro	Gly 250	Pro	Pro	Gly	Ile	Pro 255	Gly
Arg	Asn	Gly	Asp 260	Pro	Gly	Ile	Pro	Gly 265	Gln	Pro	Gly	Ser	Pro 270	Gly	Ser
Pro	Gly	Pro 275	Pro	Gly	Ile	Cys	Glu 280	Ser	Cys	Pro	Thr	Gly 285	Pro	Gln	Asn
	Ser 290	Pro	Gln	Tyr	Asp	Ser 295	Tyr	Asp	Val	Lys	Ser 300	Gly	Val	Ala	Val
Gly 305	Gly	Leu	Ala	Gly	Tyr 310	Pro	Gly	Pro	Ala	Gly 315	Pro	Pro	Gly	Pro	Pro 320
Gly :	Pro	Pro		Thr 325	Ser	Gly	His	Pro	Gly 330	Ser	Pro	Gly	Ser	Pro 335	Gly
Tyr (Gln		Pro 340	Pro	Gly (Glu		Gly 345	Gln	Ala	Gly		Ser 350	Gly	Pro

Pro Gly Pro Pro Gly Ala Ile Gly Pro Ser Gly Pro Ala Gly Lys Asp

355 360 365

Gly Glu Ser Gly Arg Pro Gly Arg Pro Gly Glu Arg Gly Leu Pro Gly 370 380

Pro Pro Gly Ile Lys Gly Pro Ala Gly Ile Pro Gly Phe Pro Gly Met 385 390 395 400

Lys Gly His Arg Gly Phe Asp Gly Arg Asn Gly Glu Lys Gly Glu Thr 405 410 415

Gly Ala Pro Gly Leu Lys Gly Glu Asn Gly Leu Pro Gly Glu Asn Gly
420 425 430

Ala Pro Gly Pro Met Gly Pro Arg Gly Ala Pro Gly Glu Arg Gly Arg
435
440
445

Pro Gly Leu Pro Gly Ala Ala Gly Ala Arg Gly Asn Asp Gly Ala Arg 450 455 460

Gly Ser Asp Gly Gln Pro Gly Pro Pro Gly Pro Pro Gly Thr Ala Gly 465 470 475 480

Phe Pro Gly Ser Pro Gly Ala Lys Gly Glu Val Gly Pro Ala Gly Ser 485 490 495

Pro Gly Ser Asn Gly Ala Pro Gly Gln Arg Gly Glu Pro Gly Pro Gln 500 505 510

Gly His Ala Gly Ala Gln Gly Pro Pro Gly Pro Pro Gly Ile Asn Gly 515 520 525

Ser Pro Gly Gly Lys Gly Glu Met Gly Pro Ala Gly Ile Pro Gly Ala 530 540

Pro Gly Leu Met Gly Ala Arg Gly Pro Pro Gly Pro Ala Gly Ala Asn 545 550 555 560

Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly Glu Pro Gly Lys Asn Gly 565 570 575

Ala Lys Gly Glu Pro Gly Pro Arg Gly Glu Arg Gly Glu Ala Gly Ile 580 585 590

Pro	o GIZ	y Val 595		o GIZ	/ Ala	ı Lys	600		ı Asp	o Gly	y Lys	605	_	y Ser	r Pro
Gly	/ Glu 610		o Gly	/ Ala	a Asn	Gly 615		Pro	Gly	y Ala	a Ala 620	_	/ Glu	ı Arg	g Gly
Ala 625		Gly	r Phe	e Arg	630		Ala	Gly	Pro	635	_	· Ile	Pro	Gly	Glu 640
Lys	Gly	Prc	Ala	Gly 645		Arg	Gly	Ala	Pro 650		Pro	Ala	Gly	Pro 655	Arg
Gly	Ala	Ala	Gly 660		Pro	Gly	Arg	Asp 665		Val	Pro	Gly	Gly 670		Gly
Met	Arg	Gly 675		Pro	Gly	Ser	Pro 680	Gly	Gly	Pro	Gly	Ser 685	Asp	Gly	Lys
Pro	Gly 690	Pro	Pro	Gly	Ser	Gln 695	Gly	Glu	Ser	Gly	Arg 700	Pro	Gly	Pro	Pro
Gly 705	Pro	Ser	Gly	Pro	Arg 710	Gly	Gln	Pro	Gly	Val 715	Met	Gly	Phe	Pro	Gly 720
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Gly	Pro	Gln 755	Gly	Pro	Pro	Gly	Pro 760	Thr	Gly	Pro	Gly	Gly 765	Asp	Lys	Gly
Asp	Thr 770	Gly	Pro	Pro	Gly	Pro 775	Gln	Gly	Leu	Gln	Gly 780	Leu	Pro	Gly	Thr
Gly 785	Gly	Pro	Pro	Gly	Glu 790	Asn	Gly :	Lys	Pro	Gly 795	Glu	Pro	Gly	Pro	Lys 800
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Ala	a Pro	Gly	7 Gli 820		g Gly	Pro	Pro	825		ı Ala	Gly	/ Ala	830		/ Leu
Arg	g Gly	/ Gly 835		a Gly	/ Pro	Pro	61y 840		Glu	ı Gly	Gly	2 Lys 845	_	Ala	a Ala
GlΣ	/ Pro 850		Gl _y	/ Pro	Pro	Glý 855		Ala	Gly	Thr	Prc 860		Leu	Gln	Gly
Met 865		Gly	Glu	ı Arg	Gly 870	Gly	Leu	Gly	Ser	Pro 875		Pro	Lys	Gly	Asp 880
Lys	Gly	Glu	Pro	885		Pro	Gly	Ala	Asp 890		Val	Pro	Gly	Lys 895	Asp
Gly	Pro	Arg	Gly 900		Thr	Gly	Pro	Ile 905	Gly	Pro	Pro	Gly	Pro 910	Ala	Gly
Gln	Pro	Gly 915	Asp	Lys	Gly	Glu	Gly 920	Gly	Ala	Pro	Gly	Leu 925	Pro	Gly	Ile
Ala	Gly 930	Pro	Arg	Gly	Ser	Pro 935	Gly	Glu	Arg	Gly	Glu 940	Thr	Gly	Pro	Pro
Gly 945	Pro	Ala	Gly	Phe	Pro 950	Gly	Ala	Pro	Gly	Gln 955	Asn	Gly	Glu	Pro	Gly 960
Gly	Lys	Gly	Glu	Arg 965	Gly	Ala	Pro	Gly	Glu 970	Lys	Gly	Glu	Gly	Gly 975	Pro
Pro	Gly	Val	Ala 980	Gly	Pro	Pro	Gly	Gly 985	Ser	Gly	Pro	Ala	Gly	Pro	Pro

- P:
- Gly Pro Gln Gly Val Lys Gly Glu Arg Gly Ser Pro Gly Gly Pro Gly
- Ala Ala Gly Phe Pro Gly Ala Arg Gly Leu Pro Gly Pro Pro Gly
- Ser Asn Gly Asn Pro Gly Pro Pro Gly Pro Ser Gly Ser Pro Gly

Lys Asp Gly Pro Pro Gly Pro Ala Gly Asn Thr Gly Ala Pro Gly Ser Pro Gly Val Ser Gly Pro Lys Gly Asp Ala Gly Gln Pro Gly Glu Lys Gly Ser Pro Gly Ala Gln Gly Pro Pro Gly Ala Pro Gly Pro Leu Gly Ile Ala Gly Ile Thr Gly Ala Arg Gly Leu Ala Gly Pro Pro Gly Met Pro Gly Pro Arg Gly Ser Pro Gly Pro Gln Gly . Val Lys Gly Glu Ser Gly Lys Pro Gly Ala Asn Gly Leu Ser Gly Glu Arg Gly Pro Pro Gly Pro Gln Gly Leu Pro Gly Leu Ala Gly Thr Ala Gly Glu Pro Gly Arg Asp Gly Asn Pro Gly Ser Asp Gly Leu Pro Gly Arg Asp Gly Ser Pro Gly Gly Lys Gly Asp Arg Gly Glu Asn Gly Ser Pro Gly Ala Pro Gly Ala Pro Gly His Pro Gly Pro Pro Gly Pro Val Gly Pro Ala Gly Lys Ser Gly Asp Arg Gly Glu Ser Gly Pro Ala Gly Pro Ala Gly Ala Pro Gly Pro Ala Gly Ser Arg Gly Ala Pro Gly Pro Gln Gly Pro Arg Gly Asp Lys Gly Glu Thr Gly Glu Arg Gly Ala Ala Gly Ile Lys Gly His Arg Gly

Phe Pro Gly Asn Pro Gly Ala Pro Gly Ser Pro Gly Pro Ala Gly

1250	1255	1260

- Gln Gln Gly Ala Ile Gly Ser Pro Gly Pro Ala Gly Pro Arg Gly 1265 1270 1275
- Pro Val Gly Pro Ser Gly Pro Pro Gly Lys Asp Gly Thr Ser Gly 1280 1285 1290
- His Pro Gly Pro Ile Gly Pro Pro Gly Pro Arg Gly Asn Arg Gly 1295 1300 1305
- Glu Arg Gly Ser Glu Gly Ser Pro Gly His Pro Gly Gln Pro Gly 1310 1315 1320
- Pro Pro Gly Pro Pro Gly Ala Pro Gly Pro Cys Cys Gly Gly Val 1325 1330 1335
- Gly Ala Ala Ile Ala Gly Ile Gly Glu Lys Ala Gly Gly 1340 1345 1350
- Phe Ala Pro Tyr Tyr Gly Asp Glu Pro Met Asp Phe Lys Ile Asn 1355 1360 1365
- Thr Asp Glu Ile Met Thr Ser Leu Lys Ser Val Asn Gly Gln Ile 1370 1380
- Glu Ser Leu Ile Ser Pro Asp Gly Ser Arg Lys Asn Pro Ala Arg 1385 1390 1395
- Asn Cys Arg Asp Leu Lys Phe Cys His Pro Glu Leu Lys Ser Gly 1400 1410
- Glu Tyr Trp Val Asp Pro Asn Gln Gly Cys Lys Leu Asp Ala Ile 1415 1420 1425
- Lys Val Phe Cys Asn Met Glu Thr Gly Glu Thr Cys Ile Ser Ala 1430 1435 1440
- Asn Pro Leu Asn Val Pro Arg Lys His Trp Trp Thr Asp Ser Ser 1445 1450 1455
- Ala Glu Lys Lys His Val Trp Phe Gly Glu Ser Met Asp Gly Gly 1460 1465 1470

Phe Gln Phe Ser Tyr Gly Asn Pro Glu Leu Pro Glu Asp Val Leu 1475 1480 Asp Val Gln Leu Ala Phe Leu Arg Leu Leu Ser Ser Arg Ala Ser 1490 1495 Gln Asn Ile Thr Tyr His Cys Lys Asn Ser Ile Ala Tyr Met Asp 1510 Gln Ala Ser Gly Asn Val Lys Lys Ala Leu Lys Leu Met Gly Ser 1520 1525 Asn Glu Gly Glu Phe Lys Ala Glu Gly Asn Ser Lys Phe Thr Tyr 1535 1540 1545 Thr Val Leu Glu Asp Gly Cys Thr Lys His Thr Gly Glu Trp Ser 1550 1555 1560 Lys Thr Val Phe Glu Tyr Arg Thr Arg Lys Ala Val Arg Leu Pro 1565 1570 1575 Ile Val Asp Ile Ala Pro Tyr Asp Ile Gly Gly Pro Asp Gln Glu 1580 1585 Phe Gly Val Asp Val Gly Pro Val Cys Phe Leu 1595 1600 <210> 15 <211> 37 <212> DNA <213> Artificial Sequence <220> <223> PCR primer <400> 15 cttgtagatg cggccgcatg aagtccagcg gcctctt 37 <210> 16 <211> 30 <212> DNA <213> Artificial Sequence <220> <223> PCR primer

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<211> 4719

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA molecule based on procollagen type III N-propeptide. Procollagen type III N-propeptide sequence replaced with the sequence for SLPI whilst retaining the collagen III signal sequence.

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<212> PRT

<213> Artificial Sequence

<220>

<223> Sequence of modified pro-alpha chain.

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Pro Glu Cys Gln Ser Asp Trp Gln Cys Pro Gly Lys Lys Arg Cys Cys 50 55 60

Pro Asp Thr Cys Gly Ile Lys Cys Leu Asp Pro Val Asp Thr Pro Asn 65 70 75 80

Pro Thr Arg Arg Lys Pro Gly Lys Cys Pro Val Thr Tyr Gly Gln Cys 85 90 95

Leu Met Leu Asn Pro Pro Asn Phe Cys Glu Met Asp Gly Gln Cys Lys
100 105 110

Arg Asp Leu Lys Cys Cys Met Gly Met Cys Gly Lys Ser Cys Val Ser 115 120 125

Pro Val Lys Ala Ala Val Glu Gly Gly Cys Ser His Leu Gly Gln Ser 130 135 140

Tyr Ala Asp Arg Asp Val Trp Lys Pro Glu Pro Cys Gln Ile Cys Val 145 150 155 160

Cys Asp Ser Gly Ser Val Leu Cys Asp Asp Ile Ile Cys Asp Asp Gln 165 170 175

Glu Leu Asp Cys Pro Asn Pro Glu Ile Pro Phe Gly Glu Cys Cys Ala 180 185 190

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Gly	/ Pro 210		n Gly	y Pro) Lys	Gly 215		Pro	Gly	r Pro	220		' Ile	Pro	Gly
Arc 225		ı Gly	/ Asp	Pro	Gly 230		Pro	Gly	Gln	Pro 235	_	Ser	Pro	Gly	Ser 240
Pro	Gly	Pro	Pro	Gly 245		Cys	Glu	Ser	Cys 250		Thr	Gly	Pro	Gln 255	Asn
Tyr	Ser	Pro	Glr 260	_	Asp	Ser	Tyr	Asp 265		Lys	Ser	Gly	Val 270	Ala	Val
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- Phe Pro Gly Ser Pro Gly Ala Lys Gly Glu Val Gly Pro Ala Gly Ser 450 455 460
- Pro Gly Ser Asn Gly Ala Pro Gly Gln Arg Gly Glu Pro Gly Pro Gln 465 470 475 480
- Gly His Ala Gly Ala Gln Gly Pro Pro Gly Pro Pro Gly Ile Asn Gly
 485 490 495
- Ser Pro Gly Gly Lys Gly Glu Met Gly Pro Ala Gly Ile Pro Gly Ala 500 505 510
- Pro Gly Leu Met Gly Ala Arg Gly Pro Pro Gly Pro Ala Gly Ala Asn 515 520 525
- Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly Glu Pro Gly Lys Asn Gly 530 540
- Ala Lys Gly Glu Pro Gly Pro Arg Gly Glu Arg Gly Glu Ala Gly Ile 545 550 555 560
- Pro Gly Val Pro Gly Ala Lys Gly Glu Asp Gly Lys Asp Gly Ser Pro 565 570 575
- Gly Glu Pro Gly Ala Asn Gly Leu Pro Gly Ala Ala Gly Glu Arg Gly 580 585 590
- Ala Pro Gly Phe Arg Gly Pro Ala Gly Pro Asn Gly Ile Pro Gly Glu
 595 600 605
- Lys Gly Pro Ala Gly Glu Arg Gly Ala Pro Gly Pro Ala Gly Pro Arg 610 615 620
- Gly Ala Ala Gly Glu Pro Gly Arg Asp Gly Val Pro Gly Gly Pro Gly 625 630 635 640
- Met Arg Gly Met Pro Gly Ser Pro Gly Gly Pro Gly Ser Asp Gly Lys 645 650 655

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Gly Gly Gly	Pro 1010 Val 1025 Ser 1040	995 Pro Ser Pro	Gly Gly Gly	Pro Pro Ala	Ala Lys Gln Thr	Gly 103 Gly 104! Gly 1066	As: 5 As: 0 Pro 5 Ala	n Th p Al p Pro	r Gl	y Ala y Ala	a Pro 10: n Pro 10: a Pro 10:	100 20 35 35 36 36 37 37 37 37 37 37 37 37 37 37	ly S ly G	er I	Pro Lys Leu

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- Gly Glu Pro Gly Arg Asp Gly Asn Pro Gly Ser Asp Gly Leu Pro 1115 1120 1125
- Gly Arg Asp Gly Ser Pro Gly Gly Lys Gly Asp Arg Gly Glu Asn 1130 1135 1140
- Gly Ser Pro Gly Ala Pro Gly Ala Pro Gly His Pro Gly Pro Pro 1145 1150 1155
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1310 1	.315	1320
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- Pro Tyr Tyr Gly Asp Glu Pro Met Asp Phe Lys Ile Asn Thr Asp 1325 1330 1335
- Glu Ile Met Thr Ser Leu Lys Ser Val Asn Gly Gln Ile Glu Ser 1340 1345 1350
- Leu Ile Ser Pro Asp Gly Ser Arg Lys Asn Pro Ala Arg Asn Cys 1355 1360 1365
- Arg Asp Leu Lys Phe Cys His Pro Glu Leu Lys Ser Gly Glu Tyr 1370 1375 1380
- Trp Val Asp Pro Asn Gln Gly Cys Lys Leu Asp Ala Ile Lys Val 1385 1390 1395
- Phe Cys Asn Met Glu Thr Gly Glu Thr Cys Ile Ser Ala Asn Pro 1400 1405 1410
- Leu Asn Val Pro Arg Lys His Trp Trp Thr Asp Ser Ser Ala Glu 1415 1420 1425
- Lys Lys His Val Trp Phe Gly Glu Ser Met Asp Gly Gly Phe Gln 1430 1435 1440
- Phe Ser Tyr Gly Asn Pro Glu Leu Pro Glu Asp Val Leu Asp Val 1445 1450 1455
- Gln Leu Ala Phe Leu Arg Leu Leu Ser Ser Arg Ala Ser Gln Asn 1460 1465 1470
- Ile Thr Tyr His Cys Lys Asn Ser Ile Ala Tyr Met Asp Gln Ala 1475 1480 1485
- Ser Gly Asn Val Lys Lys Ala Leu Lys Leu Met Gly Ser Asn Glu 1490 1495 1500
- Gly Glu Phe Lys Ala Glu Gly Asn Ser Lys Phe Thr Tyr Thr Val 1505 1510 1515
- Leu Glu Asp Gly Cys Thr Lys His Thr Gly Glu Trp Ser Lys Thr 1520 1530

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Val Asp Val Gly Pro Val Cys Phe Leu
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